

What is claimed is:

1. A cysteine variant of a member of the GH supergene family comprising a cysteine residue substituted for an amino acid selected from the group consisting of an amino acid in the loop regions, an amino acid near the ends of the alpha helices, an amino acid proximal to the first amphipathic helix, and an amino acid distal to the final amphipathic helix or wherein the cysteine residue is added at the N-terminus or C-terminus of the proteins.
2. A cysteine variant of a member of the GH supergene family comprising a cysteine residue introduced between two amino acids in the loop regions, the ends of the alpha helices, proximal to the first amphipathic helix, or distal to the final amphipathic helix.
3. A cysteine variant according to claim 1 wherein the amino acid substituted for is part of an N- or O-linked glycosylation site.
4. A cysteine variant according to claim 2 wherein the cysteine residue is introduced between two amino acids in an N-linked glycosylation site or adjacent to an amino acid in an N-linked or O-linked glycosylation site.
5. A cysteine variant according to claims 1-4 wherein the member of the GH supergene family is selected from the group consisting of growth hormone, prolactin, placental lactogen, erythropoietin, thrombopoietin, interleukin-2, interleukin-3, interleukin-4, interleukin-5, interleukin-6, interleukin-7, interleukin-9, interleukin-10, interleukin-11, interleukin-12 (p35 subunit), interleukin-13, interleukin-15, oncostatin M, ciliary neurotrophic factor, leukemia inhibitory factor, alpha interferon, beta interferon, gamma interferon, omega interferon, tau interferon, granulocyte-colony stimulating factor, granulocyte-macrophage colony stimulating factor, cardiotrophin-1 and macrophage colony stimulating factor.
6. A cysteine variant according to claim 1 wherein the amino acid substituted for is in the A-B loop, the B-C loop, the C-D loop or D-E loop of interferon/interferon-10-like members of the GH supergene family.

7. A cysteine variant according to claim 2 wherein the loop region is the A-B loop, the B-C loop, the C-D loop or D-E loop of interferon/interferon-10-like members of the GH supergene family.
- 5 8. A cysteine variant according to claims 1-7 wherein the added cysteine is PEGylated.
9. A cysteine variant according to claim 1 wherein the member of the GH supergene family is growth hormone.
- 10 10. The cysteine variant according to claim 9 wherein the substituted for amino acid is selected from the group consisting of amino acids located at the N-terminal end of the A-B loop, the B-C loop, the C-D loop, the first three or last three amino acids in the A, B, C and D helices and the amino acids proximal to helix A and distal to helix D.
- 15 11. The cysteine variant according to claim 10 wherein the substituted for amino acid is selected from the group consisting of F1, T3, P5, E33, A34, K38, E39, Q40, S43, Q46, N47, P48, Q49, T50, S51, S55, T60, A98, N99, S100, G104, A105, S106, E129, D130, G131, S132, P133, T135, G136, Q137, K140, Q141, T142, S144, K145, D147, T148, N149, S150, H151, N152, D153, S184, E186, G187, S188, and G190.
- 20 12. A cysteine variant according to claim 1 wherein the member of the GH supergene family is erythropoietin.
13. The cysteine variant according to claim 12 wherein the substituted for amino acid is
- 25 selected from the group consisting of amino acids located in the A-B loop, the B-C loop, the C-D loop, the amino acids proximal to helix A and distal to helix D and the N- or C-terminus.
14. A cysteine variant according to claim 13 wherein the substituted for amino acid is selected
- 30 from the group consisting of serine-126, N24, I25, T26, N38, I39, T40, N83, S84, A1, P2, P3, R4, D8, S9, T27, G28, A30, E31, H32, S34, N36, D43, T44, K45, N47, A50, K52, E55, G57, Q58, G77, Q78, A79, Q86, W88, E89, T107, R110, A111, G113, A114, Q115,

K116, E117, A118, S120, P121, P122, D123, A124, A125, A127, A128, T132, K154, T157, G158, E159, A160, T163, G164, D165, R166 and S85.

15. A cysteine variant according to claim 2 wherein the member of the GH supergene family
5 is growth hormone.
16. A cysteine variant according to claim 15 wherein the cysteine is introduced into the region
selected from the group consisting of amino acids located at the N-terminal end of the A-
B loop, the B-C loop, the C-D loop, the first three or last three amino acids in the A, B, C
10 and D helices and the amino acids proximal to helix A and distal to helix D.
17. A cysteine variant according to claim 2 wherein the member of the GH supergene family
is erythropoietin.
18. A cysteine variant according to claim 17 wherein the cysteine is introduced into the region
15 selected from the group consisting of the N-terminal end of the A-B loop, the B-C loop,
the C-D loop, the area of the first three or last three amino acids in the A, B, C and D
helices and proximal to helix A and distal to helix D.
19. A cysteine variant according to claim 2 wherein the member of the GH supergene family
20 is alpha interferon.
20. A cysteine variant according to claim 19 wherein the cysteine is introduced into the region
selected from the group consisting of the N-terminal end of the A-B loop, the B-C loop,
25 the C-D loop, the area of the first three or last three amino acids in the A, B, C and D
helices and proximal to helix A and distal to helix D.
21. A cysteine variant according to claim 2 wherein the member of the GH supergene family
is granulocyte-colony stimulating factor.
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22. A cysteine variant according to claim 21 wherein the cysteine is introduced into the region
selected from the group consisting of the N-terminal end of the A-B loop, the B-C loop,

the C-D loop, the area of the first three or last three amino acids in the A, B, C and D helices and proximal to helix A and distal to helix D.

23. A cysteine variant according to claims 8-22 wherein the added cysteine is PEGylated.

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